

LETTER

## Drug-Induced Acute Pancreatitis Associated with 22-Oxacalcitriol Ointment for Treatment of Psoriasis

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Dear Sir:

Hypercalcemia is usually caused by malignancies or primary hyperparathyroidism, and only rarely by drugs [1]. Hypercalcemia can occasionally cause acute pancreatitis [2]. We herein report a case of severe acute pancreatitis induced by hypercalcemia which developed as a reaction to ointment containing 22-oxacalcitriol, a vitamin D<sub>3</sub> analogue. A 72-year-old Japanese man with more than a 50-year history of psoriasis vulgaris developed generalized pustular psoriasis, which was refractory to combination therapy with corticosteroid and 22-oxacalcitriol ointments. He was referred to the Dermatology Dept. for further treatment. The patient's clinical course is shown in Figure 1. Oral etretinate, an aromatic retinoid, was started, and the 22-oxacalcitriol ointment regimen was increased soon after admission. On hospital day 13, the skin lesions improved, but the patient developed abdominal discomfort and anorexia. As laboratory data showed an increased serum level of calcium (13.2 mg/dL; reference range: 8.7-10.0 mg/dL), the ointment was immediately discontinued. On hospital day 16, the patient developed severe abdominal pain, and was referred to the Gastroenterology Dept. for further evaluation and treatment. He had no history of trauma, abdominal surgery (except for an appendectomy) or biliary disease. Laboratory data showed leucocytosis (27,070  $\mu\text{L}^{-1}$ ; reference range: 3,590-9,640  $\mu\text{L}^{-1}$ ) and increased serum amylase levels (1,040 IU/L; reference range: 39-108 IU/L), lipase (114 IU/L; reference range:

0-41 IU/L), calcium (11.3 mg/dL) and CRP (27.6 mg/dL; reference range: 0-0.3 mg/dL) levels. The level of intact parathyroid hormone (PTH) was at the lower limit of the reference range (10 pg/mL; reference range 10-65 pg/mL) and PTH-related peptide was negative. Abdominal CT showed acute edematous pancreatitis with fluid collection in the peripancreas and prerenal space, but no evidence of gallbladder disease, bile duct dilatation or malignancies. In addition to the discontinuation of the 22-oxacalcitriol ointment, we administered an antibiotic and a protease inhibitor. This conservative treatment resulted in clinical and biochemical improvement. He has since been followed up for 11 months without any signs of recurrence. Topical vitamin D<sub>3</sub> analogues are a well-established treatment for psoriasis [3]. Hypercalcemia has been reported as a serious adverse effect of these analogues but, in fact, many patients who develop such hypercalcemia are found to have exceeded the recommended dose regimen [4, 5, 6]. In our patient, in addition to long-term corticosteroid use and excessive

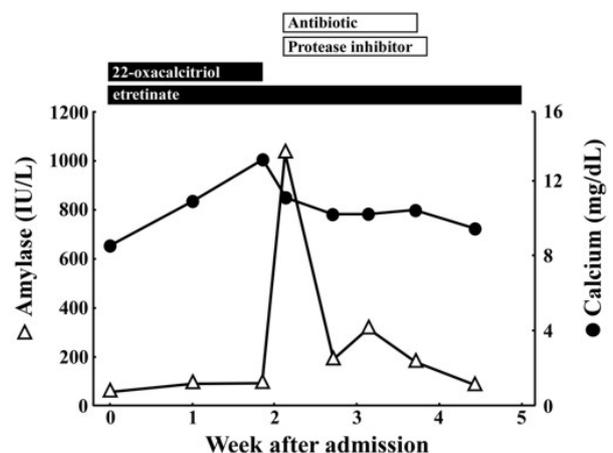


Figure 1. Serum levels of calcium (reference range: 8.7-10.0 mg/dL) and amylase (reference range: 39-108 IU/L) during the course of hospitalization.

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application of 22-oxacalcitriol, oral etretinate had been used for pustular psoriasis, which altered the barrier function of the skin due to severe inflammation. It is known that oral administration of retinoids can impair skin barrier function and cause hypertriglyceridemia as a cause of acute pancreatitis [7, 8]. In our case, there is no evidence of hypertriglyceridemia during the course of hospitalization. Accordingly, we speculated that the resulting dramatic increase of 22-oxacalcitriol absorption through the skin had caused the hypercalcemia, thereby leading to acute pancreatitis. A disturbance in calcium metabolism is associated with acute pancreatitis. Marked hypocalcemia is a grave prognostic sign of acute pancreatitis while hypercalcemia is a known etiologic factor of acute pancreatitis. The relationship between hypercalcemia and acute pancreatitis remains controversial, although several theories have been proposed [9, 10]. Among the forms of organ damage due to hypercalcemia, acute pancreatitis is a rare but potentially lethal one. Therefore, it is vital to check calcium levels regularly in patients with severe psoriasis who are using vitamin D<sub>3</sub> analogues, especially when combined with corticosteroid and/or retinoid.

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**Conflict of interest** The authors have no potential conflicts of interest

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